

REMARKS

Upon entry of this Amendment, Claims 1-2 and 9-13 will be pending. Claims 9-12 are hereby amended and Claim 4 is hereby canceled without prejudice or disclaimer as to the underlying subject matter. Support for the amended claims may be found throughout the Specification. See, for example, Specification at page 9, line 18 - page 10, line 7; page 10, line 16 - page 11, line 19; and page 14, lines 14-19. No new matter is added by way of these amendments.

Applicants would like to thank the Examiner for withdrawing the rejections of Claims 4, 9-12 over 35 U.S.C. § 112, first paragraph, and the rejection of Claims 4 and 9-13 over 35 U.S.C. § 102(b).

I. Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 4, and 9-12 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly “being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” Final Office Action at page 2. In rejecting the claims, the Examiner asserts that the terms “high stringency” and “at least about” are unclear. *Id.*

Applicants disagree with the Examiner’s assertion but have amended the claims without prejudice or disclaimer solely in order to facilitate prosecution. As such, Applicants respectfully request withdrawal of the rejection.

II. Rejection under 35 U.S.C. §101

Claims 1, 2, 4 and 9-13 stand rejected under 35 U.S.C. § 101, because the claimed invention allegedly lacks patentable utility. Final Office Action at page 3. The Examiner further alleges that “the claimed invention is not supported by either a substantial, specific asserted utility or a well established utility.” *Id.* Applicants disagree.

In *In re Fisher*, the Federal Circuit reiterated that the “basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived from the public from an invention with *substantial utility*.” *In re Fisher*, 421 F.3d 1365, 1371 (Fed.

Cir. 2005) (citing *Brenner v. Manson*, 383 U.S. at 534-35, 1966) (emphasis in original). The Court noted that since “*Brenner* our predecessor court, the Court of Customs and Patent Appeals, and this court have required a claimed invention to have a specific and substantial utility to satisfy §101.” *Id.* Furthermore, an invention need only provide one identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958 (Fed. Cir. 1983) (“when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown”).

Although the Supreme Court has not defined the meaning of the terms “specific” and “substantial”, the Federal Circuit has identified a framework for the kind of disclosure an application could contain to establish a specific and substantial utility. *In re Fisher*, 421 F.3d at 1371. First, the Court indicated that to provide a substantial utility, the specification should disclose a utility such that “one skilled in the art can use a claimed discovery in a manner which provides some *immediate benefit to the public*.” *Id.* (emphasis in original). Second, a specific utility can be disclosed by discussing “a use which is not so vague as to be meaningless,” that is that the claimed invention “can be used to provide a well-defined and particular benefit to the public.” *Id.*

Applicants disagree with the Examiner’s assertion that the arguments presented in the July 14, 2008 response do not establish a utility for SEQ ID NO: 3366. Final Office Action at page 3. Applicants also disagree with the Examiner’s assertion that “absent guidance on how SEQ ID NO: 3366 can be used to achieve an immediate and specific benefit, the claimed invention lacks substantial, specific asserted utility.” *Id.* In reaching this conclusion, the Examiner fails to acknowledge that Table 1 indicates that SEQ ID NO: 3366 is a member of the cytochrome p450 family and exhibits a strong correlation to a number of cytochrome p450 family members, such as Accession No. AY050980 and Accession No. AY091446. Alone, the disclosure of Table 1 in the specification establishes that SEQ ID NO: 3366 has substantial, specific, and well-established utility and is sufficient to satisfy the utility requirement under 35 U.S.C. § 101.

As set forth in the Response submitted July 14, 2008, the utility of SEQ ID NO: 3366 is further demonstrated by a BLASTN analysis. The specification as filed discloses that a BLASTN analysis is well-known and conventional techniques that can be used to obtain information about nucleic acid sequences. Specification, for example, at page 4 - page 22, line 12; page 42, line 18 - page 46, line 16; and Example 2. The results of a BLASTN analysis of SEQ ID NO: 3366 demonstrate a strong correlation between SEQ ID NO:3366 and numerous well-established cytochrome p450 sequences. For example, as provided in the Information Disclosure Statement submitted on July 14, 2008, at least the following sequences exhibit a greater than 54% percent identity to SEQ ID NO: 3366 together with a well-established utility as a cytochrome p450 protein: Accession No. NM118043, Accession No. AY091446, Accession No. AY050980, Accession No. AB122149, Accession No. NM202845, Accession No. NM123902, Accession No. NM180805, and Accession No. AB122150. However, the Examiner ignores this in rejecting the claims.

The Examiner also ignores Applicants arguments regarding SEQ ID NO: 6915 in the Office Action. As set forth in the response submitted July 14, 2008, the results of a BLASTP analysis of the elected corresponding amino acid sequence, SEQ ID NO: 6915, also demonstrates a strong correlation between SEQ ID NO: 6915 and numerous well-established cytochrome p450 sequences. For example, as provided in the Information Disclosure Statement submitted on July 14, 2008, at least the following sequences exhibit a greater than 54% percent identity to SEQ ID NO: 6915 together with a well-established utility as a cytochrome p450 protein: Accession No. NP001047855, Accession No. Q05JG2, Accession No. NP567581, Accession No. NP851136, Accession No. CAA16713, Accession No. NP974574, Accession No. NP199347, Accession No. NP566628, Accession No. NP974574, Accession No. NP180473, Accession No. AAZ23260, Accession No. BAD38475, and Accession No. Q09J78.

As confirmed by BLASTN and BLASTP searches, there are a number of well-known cytochrome p450 sequences that exhibit a greater than 54% percent identity to both SEQ ID NO: 3366 and SEQ ID NO: 6915. The above BLAST analysis complements Table 1 of the specification which indicates that SEQ ID NO: 3366 is a member of the cytochrome p450 family and exhibits a strong correlation to a number of cytochrome p450 family members. Applicants

respectfully submit that the results of the BLASTN and BLASTP analysis demonstrate that both SEQ ID NO: 3366 and SEQ ID NO: 6915 have utilities specific to them and not generally applicable to any nucleotide and amino acid sequence, respectively. These utilities are credible, substantial, and well-established; they are neither vague nor impractical. Applicants need only establish a single utility to satisfy 35 U.S.C. § 101, and have done so in the present case.

Moreover, as set forth in the response submitted July 14, 2008, an article by Werck-Reichhart *et al.* indicates that “[s]equence identity among P450 proteins is often extremely low and may be less than 20% and there are only three absolutely conserved amino acid.” “Cytochromes P450: a success story,” *Genome Biology*, 1 reviews, 3003.1-3003.9, at page 3002.2, December 8, 2000. Further, according to Werck-Reichhart *et al.*, the amino-acid sequence of the cytochrome p450 family is “extremely diverse, with levels of identity as low as 16% in some cases.” *Id.* at abstract. At a minimum, this indicates that the greater than 54% sequence identity between both SEQ ID NO: 3366 and SEQ ID NO: 6915 and well-known cytochrome p450 sequences is more than sufficient to satisfy the utility requirement under 35 U.S.C. § 101.

Furthermore, the claimed DNA sequence, SEQ ID NO: 3366, and the corresponding claimed amino acid sequence, SEQ ID NO: 6915, contain many of the same structural motifs of cytochrome P450 proteins as set forth in Werck-Reichhart *et al.* For one, SEQ ID NO: 6915 includes “Glu Thr Met Arg” at amino acid positions 339-342 as well as “Pro Leu Pro Pro” at amino acid positions 38-41 which are noted by Werck-Reichhart *et al.* as being a hallmarks of cytochrome p450 proteins.¹ Werck-Reichhart *et al.* at page 3003.2, second column, and Figures 1-2. Further, SEQ ID NO: 6915 includes the “Phe Gly Asn Gly Thr His Ser Cys Pro Gly” motif at amino acids positions 408 - 417 which contains the Cys residue which is described by Werck-Reichhart *et al.* as being important as a ligand to heme iron.² *Id.* With this, one of skill in the art

¹ As set forth in Werck-Reichhart *et al.*, a hallmark of cytochrome p450 proteins is a “Glu-X-X-Arg motif in helix K” and “cluster of prolines (Pro-Pro-X-Pro).” Werck-Reichhart *et al.* at page 3003.2, column 2, and Figures 1-2.

² As set forth in Werck-Reichhart *et al.*, a hallmark of cytochrome p450 proteins is a “(Phe-X-X-Gly-X-Arg-X-Cys-X-Gly), located on the proximal face of the heme just before the L helix, with the absolutely conserved cysteine that serves as fifth ligand to the heme iron.” *Id.*

would fully appreciate that SEQ ID NO: 3366 and SEQ ID NO: 6915 would have utility as cytochrome p450 proteins.

The present application provides utilities for the claimed polypeptides that are well-defined and provide an immediate benefit to the public. The fact that the claimed nucleotide and amino acid sequences exhibits a high correlation to cytochrome p450 proteins is more than ample to support the specific utilities asserted in the specification. Moreover, there are numerous other utilities asserted in the specification regarding nucleotide sequence SEQ ID NO: 3366 and amino acid sequence SEQ ID NO: 6915. Specification at page 6, line 10-17; page 7, line 23 - page 8, lines 17; page 12, line 13 - page 13, line 13; page 14, line 20 - page 15, line 2; page 15, line 12 - 21, line 3; and Table 1. Without being limited, the specification provides that the sequences of the invention can also be used for improving nitrogen yield, improving stress, heat, cold, osmotic, draught, and pest tolerance, increasing seed protein yield and content. Specification at page 15, line 22 - page 21, line 3. Any one of these asserted utilities is specific, substantial and credible under the requirements of 35 U.S.C. § 101.

Applicants respectfully remind the Examiner that the utilities asserted in the specification must be accepted as factually sound unless the Patent Office cites information that undermines the credibility of the assertion. *In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). As the Examiner is aware, “a ‘rigorous correlation’ need not be shown in order to establish practical utility; ‘reasonable correlation’ is sufficient.” *See, Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 U.S.P.Q.2d 1895, 1900 (Fed. Cir. 1996), emphasis added. “An Applicant can establish this reasonable correlation by relying on statistically relevant data documenting the activity of the compound or composition, arguments or reasoning, documentary evidence, or any combination thereof.” M.P.E.P. § 2107.03, at page 2100-43.

In conclusion, because Applicants need only establish a single utility to satisfy 35 U.S.C. § 101, and have done so with sufficient specificity and reasonable correlation in the present application, the rejection under 35 U.S.C. § 101 is incorrect and Applicants respectfully request its withdrawal.

III. Rejection Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 1, 2, 4 and 9-13 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled because the claimed invention lacks utility. Final Office Action at pages 3-4. In rejecting the claims, the Examiner asserts that “since the claimed invention is not supported by either a substantial, specific asserted utility or a well-established utility for the reasons set forth above, one skilled in the art would not know how to use he claimed invention.” Final Office Action at page 4. Applicants disagree.

Applicants submit that the rejection of Claims 1, 2, 4 and 9-13 under 35 U.S.C. § 112, first paragraph, has been overcome by the arguments set forth above with respect to the rejection under 35 U.S.C. § 101. In other words, Applicants respectfully submit that the claimed nucleic acid molecules have specific, substantial, and well-established utilities, and therefore one skilled in the art would know how to make and use the claimed invention. Applicants note that the hybridization language has been removed from Claim 4 solely in order to facilitate prosecution. Accordingly, Applicants request withdrawal of the rejection of Claims 1, 2, 4 and 9-13 under 35 U.S.C. § 112, first paragraph.

The Examiner has not met the evidentiary burden to impose an enablement rejection. A specification that discloses how to use a claimed invention “must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein.” *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995), quoting *In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original).

As the M.P.E.P. makes clear, “(t)he specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public.” M.P.E.P. § 2164.05(a). See also, *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463 (Fed. Cir. 1984). Furthermore, it is well-established patent jurisprudence that Applicants need not teach “conventional and well-known genetic

engineering techniques.” *Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345 (Fed. Cir. 2000).

Applicants disagree with the Examiner’s assertion that “Applicant’s arguments are not commensurate in scope with the claims” and “[t]he claims are limited to codon degeneracy changes and conservative amino acid substitutions.” Final Office Action at page 4. Applicants further disagree with the Examiner’s assertion that “neither the specification nor the state of the art at the time the invention was made provides guidance as to where the critical region(s) are, or what plant function SEQ ID NO: 3366 has so that its activity can be maintained.” *Id.* Applicants further disagree with the Examiner’s assertion that “[a]bsent further guidance, one skilled in the art cannot make and use the claimed invention without undue experimentation.” *Id.*

The Examiner’s position lacks both a legal and factual basis. For one, as set forth in the above response relating to the 35 U.S.C. § 101 rejections, Werck-Reichhart *et al.* provides detailed guidance regarding sequence identity and function in cytochrome p450 proteins. Specifically, Werck-Reichhart *et al.* indicates that “[s]equence identity among P450 proteins is often extremely low and may be less than 20% and there are only three absolutely conserved amino acid.” Werck-Reichhart *et al.* at page 3002.2. Moreover, the claimed DNA sequence, SEQ ID NO: 3366, and the corresponding claimed amino acid sequence, SEQ ID NO: 6915, contain many of the same structural motifs of cytochrome p450 proteins as set forth in Werck-Reichhart *et al.* For instance, SEQ ID NO: 6915 includes “Glu Thr Met Arg” at amino acid positions 339-342 as well as with “Pro Leu Pro Pro” at amino acid positions 38-41 which are noted by Werck-Reichhart *et al.* as being a hallmarks of cytochrome p450 proteins.³ Werck-Reichhart *et al.* at page 3003.2, second column, and Figures 1-2. Further, SEQ ID NO: 6915 includes the “Phe Gly Asn Gly Thr His Ser Cys Pro Gly” motif at amino acids positions 408 - 417 which contains the Cys residue which is described by Werck-Reichhart *et al.* as being

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important as a ligand to heme iron.⁴ *Id.* With this, Werck-Reichhart *et al.* provides guidance regarding the structural motifs of cytochrome p450 proteins such that one of skill in the art would have the ability to practice the claimed invention without undue experimentation.

The Examiner's rejection of the claims because the specification allegedly fails to provide "guidance as to where the critical region(s) are, or what plant function SEQ ID NO: 3366 has so that its activity can be maintained" also disregards the standard of one of ordinary skill in the art. Given at least the teachings of the specification, one of ordinary skill in the art would have the ability to make nucleotide substitutions to SEQ ID NO: 3366 and amino acid substitutions to SEQ ID NO: 6915 without undue experimentation. Performing routine and well-known steps cannot create undue experimentation even if it is laborious. *See In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976). However, the Examiner ignores this in rejecting the claims.

Applicants have provided considerable direction and guidance such that it is well within the level of ordinary skill in the art to practice the claimed invention without undue experimentation. For example, given the specification, one of skill in the art would recognize that degeneracy of the genetic code would account for nucleic acid molecules comprising different nucleotides but encoding for the same protein with the same function. Specification, for example, at page 14, lines 3-13. Moreover, one of skill in the art would also have the ability to modify the nucleic acid sequence of SEQ ID NO:3366 such that it would encode for a protein with conservative amino acid substitutions. Specification, for example, at page 22, line 12 - page 23, line 16. As provided in the specification, one of skill in the art would recognize that conservative amino acid substitution is based on a variety of well known factors and can be accomplished without undue experimentation. *Id.* For example, without being limited, one of skill in the art would have the ability to make conservative amino acid substitutions based on the charge, polarity, hydrophobicity, hydrophilicity, and relative side group of the amino acid. *Id.*

⁴ As set forth in Werck-Reichhart *et al.*, a hallmark of cytochrome p450 proteins is a "(Phe-X-X-Gly-X-Arg-X-Cys-X-Gly), located on the proximal face of the heme just before the L helix, with the absolutely conserved cysteine that serves as fifth ligand to the heme iron." *Id.*

Additionally, one of skill in the art would recognize that changes to the critical region of a protein should be handled with caution as to avoid influencing the activity of the protein. *Id.*

It is submitted that Applicants have provided considerable direction and guidance, and has presented working examples such that it is well within the level of ordinary skill in the art to practice the invention without undue experimentation. The Examiner has not provided sufficient evidence to discredit the teaching in the specification. Rather, the Examiner suggests inapplicable and generalized observations.

Accordingly, for at least these reasons, it is submitted that the claims are sufficiently enabled under 35 U.S.C. § 112, first paragraph, and withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that the present application is now in condition for allowance, and respectfully request notice of such. The Examiner is encouraged to contact the undersigned at 202-942-5000 if any additional information is necessary for allowance.

Respectfully submitted,



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